



PTO/SB/08a (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO  <b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				<b>Complete if Known</b> Application Number: 09/978,297 Filing Date: October 17, 2001 First Named Inventor: Oron JACOBY-ZEEVI Art Unit: 1652 Examiner Name: HUTSON, RICHARD G Attorney Docket Number: 01/22716	
Sheet	1	of	15		

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			
RH	1	US-4,455,296	06-19-1984	Hansen et al.	
	2	US-6,153,187	11-28-2000	Yacoby-Zeevi	
	3	US-5,145,679	08-8-1992	Hinson	
	4	US-5,736,137	07-7-1998	Anderson et al.	
	5	US-5,194,596	03-16-1993	Tischer et al.	
	6	US-5,350,836	09-27-1994	Kopchick et al.	
	7	US-5,580,862	03-3-1996	Rosen et al.	
	8	US-5,474,983	12-12-1995	Kuna et al.	
	9	US-5,618,709	08-8-1997	Gewirtz et al.	
	10	US-5,656,595	08-12-1997	Schweighoffer et al.	
	11	US-4,683,195	07-28-1987	Mullis et al.	
	12	US-5,602,095	02-11-1997	Pastan et al.	
	13	US-4,117,841	03-3-1978	Perrotta et al.	
	14	US-5,830,759	03-3-1998	Chang et al.	
	15	US-6,230,151	08-8-2001	Agrawal et al.	
	16	US-5,799,311	08-25-1998	Agrawal et al.	
	17	US-6,314,420	06-6-2001	Lang et al.	
	18	US-4,937,747	06-26-1990	Koller	
	19	US-6,307,965	10-23-2001	Aggarwal et al.	
	20	US-6,226,792	01-1-2001	Goiffon et al.	
	21	US-5,859,929	01-12-1999	Zhou et al.	
	22	US-5,799,276	08-25-1998	Komissarchik et al.	
	23	US-5,360,735	01-1-1994	Weinshank et al.	
	24	US-5,589,604	12-31-1996	Drohan et al.	
	25	US-5,700,671	12-23-1997	Prieto et al.	
	26	US-5,714,345	03-3-1998	Clark	
	27	US-5,716,817	02-10-1998	Törnelli	
	28	US-6,140,552	10-31-2000	Deboer et al.	
	29	US-6,190,875	02-20-2001	Ben-Artzi et al.	
	30	US-2001/0006630	05-5-2001	Yacobi-Zeevi et al.	
	31	US-4,859,581	08-22-1989	Nicholson et al.	
	32	US-4,882,318	11-21-1989	Vlodavsky et al.	
	33	US-5,129,877	07-14-1992	Gallo et al.	
	34	US-5,206,223	04-27-1993	Vlodavsky et al.	
	35	US-5,332,812	07-26-1994	Nicolson et al.	
	36	US-5,399,351	03-21-1995	Leshchiner et al.	
	37	US-5,550,116	08-27-1996	Lormeau et al.	
	38	US-5,667,501	09-16-1997	Fowler et al.	
	39	US-5,739,115	04-14-1998	Fugedi et al.	
	40	US-6,177,545	01-13-2001	Pecker et al.	
	41	US-4,946,778	08-8-1990	Ladner et al.	
	42	US-5,997,863	07-7-1999	Zimmermann et al.	
	43	US-6,242,238	05-5-2001	Freeman et al.	

RH

/Richard Hutson/ (09/25/2006)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO  <b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				<b>Complete if Known</b>	
				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	2	of	15	Attorney Docket Number	01/22716

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Documents	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> Number <sup>4</sup> Kind Code <sup>5</sup> (if known)				
RH	44	PCT WO 91/19197	12-12-1991	Nicolson et al.		
	45	PCT WO 97/11684	03-3-1997	Bennett et al.		
	46	PCT WO 99/18852	04-22-1999	Arenson		
	47	PCT WO 91/02977	07-7-1991	Fuks et al.		
	48	PCT WO 97/27327	07-31-1997	Van Ness et al.		
	49	PCT WO 00/52149	08-8-2000	Yacobi-Zeevi		
	50	PCT WO 00/52178	08-8-2000	Pecker et al.		
	51	PCT WO 00/52178	08-8-2000	Pecker et al.		
	52	PCT WO 99/40207	08-12-1999	Nakjima et al.		
	53	PCT WO 98/46258	10-22-1998	Bhaskar et al.		
	54	EP 0254067	01-27-1988	Cohen et al.		
	55	PCT WO 98/03638	01-29-1998	Freeman et al.		
	56	PCT WO 01/00643	04-4-2001	Pecker et al.		
	57	PCT WO 99/48478	09-30-1999	Yacoby-Zeevi		
	58	PCT WO 00/03036	01-20-2000	Ben-Artzi et al.		
	59	PCT WO 00/25817	05-11-2000	Peretz et al.		
	60	PCT WO 92/01003	01-23-1992	Nicolson et al.		
	61	AU 735116	06-28-2001	Pecker et al.		
	62	PCT WO 99/57244	11-11-1999	Ben-Artzi et al.		
	63	PCT WO 99/57153	11-11-1999	Pecker et al.		
	64	PCT WO 99/11798	03-11-1999	Pecker et al.		
	65	PCT WO 88/01280	02-25-1988	Nicolson et al.		
	66	PCT WO 95/04158	09-9-1995	Hoogewerf et al.		
RH						

Examiner Signature	/Richard Hutson/ (09/25/2006)	Date Considered
--------------------	-------------------------------	-----------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.  
SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

/Richard Hutson/ (09/25/2006)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO  <b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
Examiner Name	HUTSON, RICHARD G				
Sheet	3	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	67	Rader et al. "A Phage Display Approach for Rapid Antibody Humanization: Designed Combinatorial V Gene Libraries", Proc. Natl. Acad. Sci. USA, 95: 8910-8915, 1998.			
	68	Mateo et al. "Humanization of A Mouse Monoclonal Antibody That Blocks the Epidermal Growth Factor Receptor: Recovery Antagonistic Activity", Immunotechnology, 3: 71-81, 1997. Abstract.			
	69	Luft " Making Sense Out of Antisense Oligodeoxynucleotide Delivery: Getting There Is Half the Fun". J. Mol. Med, P.75-76. 1998.			
	70	Kronenwett et al. "Oligodeoxyribonucleotide Uptake in Primary Human Hematopoietic Cells Is Enhanced by Cationic Lipids and Depends on the Hematopoietic Cell Subset", Blood, 91(3): 852-862, 1998.			
	71	Flanagan et al. "Potent and Selective Gene Inhibition Using Antisense Oligodeoxynucleotides", Molecular and Cellular Biochemistry, 172: 213-225, 1997.			
	72	Aoki et al. "In Vivo Transfer Efficiency of Antisense Oligonucleotides Into the Myocardium Using HVJ-Liposome Method", Biochemical and Biophysical Research Communications, 231: 540-545, 1997.			
	73	Jayaraman et al. "Rational Selection and Quantitative Evaluation of Antisense Oligonucleotides", Biochimica et Biophysica Acta, 1520: 105-114, 2001.			
	74	Walton et al. "Prediction of Antisense Oligonucleotide Binding Affinity to A Structured RNA Target", Biotechnology and Bioengineering, 65(1): 1-9, 1999.			
	75	Uno et al. "Antisense-Mediated Suppression of Human Heparanase Gene Expression Inhibits Pleural Dissemination of Human Cancer Cells", Cancer Research, 61(21): 7855-7860, 2001.			
	76	Anatolii "Hyaluronic Capsule as One of the Factors of Hemolytic Streptococcus Pathogenicity", Chem. Abstracts 86(17): 339, 1977. Abstr.118714 in Zh. Mikrobiol. Epidemiol. Immunobiol., 2: 22-27, 1977.			
	77	Li et al. "Immunochemical Localization of Heparanase in Mouse and Human Melanomas", Int. J. Cancer, 45: 1088-1095, 1990.			
	78	Soule et al. "Isolation and Characterization of A Spontaneously Immortalized Human Breast Epithelial Cell Line, MCF-10", Cancer Res., 50: 6075-6086, 1990. Abstract.			
	79	Miller et al. "Xenograft Model of Progressive Human Proliferative Breast Disease", J. Nat. Cancer Inst., 85: 1725-1732, 1993. Abstract.			
	80	Nakajima et al. "Heparan Sulfate Degradation: Relation to Tumor Invasion and Metastatic Properties of Mouse B16 Melanoma Sublines", Science, 220: 611-613, 1983.			
	81	Kosir et al. "Early Human Breast Carcinoma Cells Produce Extra Cellular Heparanase", Molecular Biology/Biochemistry, Proceedings of the American Association for Cancer Research, 37: 495, 1996.			
	82	Laskov et al. "Production of Heparanase by Normal and Neoplastic Murine - B-Lymphocytes", International Journal of Cancer, 47(1): 92-98, 1991.			

RH/Richard Hutson (09/25/2006)

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. this collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount

/Richard Hutson/ (09/25/2006)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1448A/PTO				Complete if Known	
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	4	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	83	Hillier et al. "The WashU-Merck EST Project", No. N30824, Database GenBank on STN, US National Library of Medicine (Bethesda MD), 1996. Suppl. IDS in 23884;			
	84	Hillier et al. "The WashU-Merck EST Project", No. N30845, Database GenBank on STN, US National Library of Medicine (Bethesda MD), 1996.			
	85	Jusa et al. "Effect of Heparin Infection of Cells by Porcine Reproductive and Respiratory Syndrome Virus", Am. J. Vet. Res., 58(5): 488-491, 1997. Abstract.			
	86	Ducy et al. "The Osteoblast: A Sophisticated Fibroblast Under Central Surveillance", Science, 289: 1501-1504, 2000.			
	87	Reddi "Role of Morphogenetic Proteins in Skeletal Tissue Engineering and Regeneration", Nature Biotechnology, 16: 247-252, 1998.			
	88	Elkin et al. "Heparanase as Mediator of Angiogenesis: Mode of Action", The FASEB Journal, 15: 1661-1663, 2001.			
	89	Elkin et al. "Heparanase as Mediator of Angiogenesis: Mode of Action", The FASEB Journal, Published Online, 10 P. 2001.			
	90	Finkel "Potential Target Found for Antimetastasis Drugs", Science, 285: 33-34, 1999.			
	91	Webster et al. "FGFR Activation in Skeletal Disorders: Too Much of A Good Thing", TIG, 13(5): 178-182, 1997.			
	92	Shimazu et al. "Syndecan-3 and the Control of Chondrocyte Proliferation During Endochondral Ossification", Exp. Cell. Res., 229(1): 126-136, 1996. Abstract.			
	93	Blanquaert et al. "CMDBS, Functional Analogs of Sulfate Heparanes, Used as Osseous Cicatrizing Agents", Ann. Endocrinol., 55(2): 121-123, 1994. Abstract.			
	94	Blanquaert et al. "Heparan-Like Molecules Induce the Repair of Skull Defects", Bone, 17(6): 499-506, 1995. Abstract.			
	95	Muir et al. "Histomorphometric Analysis of the Effects of Standard Heparin on Trabecular Bone In Vivo", Blood, 88(4): 1314-1320, 1996. Abstract.			
	96	Hoffman et al. "Human Bone Morphogenetic Protein 2 Contains A Heparin-Binding Site Which Modifies Its Biological Activity", Eur. J. Biochem., 237(1): 295-302, 1996. Abstract.			
	97	Imai et al. "Osteoblast Recruitment and Bone Formation Enhanced by Cell Matrix-Associated Heparin-Binding Growth-Associated Molecule (HB-GAM)", J. Cell. Biol. 143(4): 1113-1128, 1998. [Abstract]			
	98	Loredo et al. "Regulation of Glycosaminoglycan Metabolism by Bone Morphogenetic Protein-2 in Equine Cartilage Explant Cultures", Am. J. Vet. Res., 57(4): 554-559, 1996.			
	99	Kiberstis et al. "Bone Health in the Balance", Science, 289: 1497, 2000.			
	100	Service "Tissue Engineers Build New Bone", Science, 289: 1498-1500, 2000.			

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>. Applicant's unique citation designation number (optional). <sup>2</sup>. Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.  
SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9189 and select option 2.

/Richard Hutson/ (09/25/2006)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO				Complete if Known	
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	5	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	101	Stracke et al. "Autotaxin, Tumor Motility-Stimulating Exophosphodiesterase", Advan. Enzyme Regul., 37: 135-144, 1997. Introduction.			
	102	Bost et al. "Antibodies Against A Peptide Sequence Within the HIV Envelope Protein Crossreacts With Human Interleukin-2", Immunol. Invest., 17: 577-586, 1988.			
	103	Bendayan "Possibilities of False Immunocytochemical Results Generated by the Use of Monoclonal Antibodies: The Example of the Anti-Proinsulin Antibody", J. Histochem. Cytochem. 43: 881-886, 1995.			
	104	Hillier et al. "The WashU-Merck EST Project" GenBank Entry N32056, 1996. Claims: 9, 10. // Suppl. IDS in 23884;			
	105	Adams et al. "Initial Assessment of Human Gene Diversity and Expression Patterns Based Upon 83 Million Nucleotides of cDNA Sequence", Nature, 377(6547): 3-174, 1995. GenBank Entry AA304653, 1997. Claims: 30.			
	106	Yagel et al. "Normal Nonmetastatic Human Trophoblast Cells Share In Vitro Invasive Properties of Malignant Cells", J. Cellular Physiology, 136: 455-462, 1988.			
	107	Edwards et al. "Some Properties and Applications of Monoclonal Antibodies", Biochem. Journal, 200: 1-10, 1981.			
	108	Zhou et al. "HFE Gene Knockout Produces Mouse Model of Hereditary Hemochromatosis", PNAS, 95(5): 2492-2497, 1998.			
	109	Menezo et al. "Mouse and Bovine Models for Human IVF", Reproductive BioMedicine Online 2002, 4(2): 170-175, 2002. Abstract.			
	110	Bean et al. "Fertilization In Vitro Increases Non-Disjunction During Early Cleavage Divisions in A Mouse Model System", Human Reproduction, 17(9): 2362-2367, 2002. Abstract.			
	111	Brinster et al. "Restoration of Fertility by Germ Cell Transplantation Requires Effective Recipient Preparation", Biology of Reproduction 69: 412-420, 2003. Abstract.			
	112	Liu et al. "Live Offspring by In Vitro Fertilization of Oocytes From Cryopreserved Primordial Mouse Follicles After Sequential In Vivo Transplantation and In Vitro Maturation", Biology of Reproduction, 64: 171-178, 2001. Abstract.			
	113	Kawase et al. "Effect of Partial Incision of the Zona Pellucida by Piezo-Micromanipulator for In Vitro Fertilization Using Frozen-Thawed Mouse Spermatozoa on the Developmental Rate of Embryos Transferred at the 2-Cell Stage", Biology of Reproduction, 66: 3810385, 2002. Abstract.			
	114	Pfaff et al. "Cryobiology of Rat Embryos I: Determination of Zygote Membrane Permeability Coefficients for Water and Cryoprotectants, Their Activation Energies, and the Development of Improved Cryopreservation Methods", Biology of Reproduction, 63: 1294-1302, 2000. Abstract.			
	115	Yesildaglar et al. "The Mouse as A Model to Study Adhesion Formation Following Endoscopic Surgery: A Preliminary Report", Human Reproduction, 14(1): 55-59, 1999. Abstract.			
	116	Ejima et al. "Induction of Apoptosis in Placentas of Pregnant Mice Exposed to Lipopolysaccharides: Possible Involvement of Fas/Fas Ligand System", Biology of Reproduction, 62: 178-185, 2000. Abstract.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>. Applicant's unique citation designation number (optional). <sup>2</sup>. Applicant is to place a check mark here if English language Translation is attached.

/Richard Hutson/ (09/25/2006)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO				Complete if Known	
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	6	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	117	Pralhada et al. "Diethylstilbestrol-Induced Cervical and Vaginal Adenosis Using the Neonatal Mouse Model", Biology of Reproduction, 38: 935-943, 1988. Abstract.			
	118	Newbold et al. "Exposure to Diethylstilbestrol During Pregnancy Permanently Alters the Ovary and Oviduct", Biology of Reproduction, 28: 735-744, 1983. Abstract.			
	119	??? "Mouse Models for Reproductive Biology Research" - www.jax.org/jaxmice : 1-2, Summer 2002.			
	120	Jin et al. "Molecular Cloning and Expression of Human Heparanase cDNA", Proceedings American Association for Cancer Research Annual Meeting, 1992, 33: 57, 1992. Abstract. Suppl. S18 in 21782; AU/OA:30.11.05 in 27517/30.11.05 in 27440; Suppl. IDS in 27970; IDS in 26871; IDS in 25718; Suppl. IDS in 23884;			
	121	Thuong et al. "Sequence-Specific Recognition and Modification of Double-Helical DNA by Oligonucleotides", Angew.Chem. Int. Ed. Engl. 32: 666-690, 1993.			
	122	Cohen "Oligonucleotide Therapeutics", Trends in Biotechnology 10: 87-91, 1992. Abstract.			
	123	Szczylik et al. "Selective Inhibition of Leukemia Cell Proliferation by BCR-ABL Antisense Oligodeoxynucleotides", Science, 253: 562-565, 1991. Abstract.			
	124	Calabretta et al. "Normal and Leukemic Hematopoietic Cell Manifest Differential Sensitivity to Inhibitory Effects of C-myc Antisense Oligodeoxynucleotides: An In Vitro Study Relevant to Bone Marrow Purging", Proc. Natl. Acad. Sci. USA, 88: 2351-2355, 1991.			
	125	Burch et al. "Oligodeoxynucleotides Antisense to the Interleukin 1 Receptor mRNA Block the Effects of Interleukin 1 in Cultured Murine and Human Fibroblasts and in Mice", J. Clin. Invest., 88: 1190, 1991. Abstract.			
	126	Agrawal "Antisense Oligonucleotides as Antiviral Agents", Trends Biotechnol., 10(5): 152-158, 1992. Abstract.			
	127	Ferber et al. "Pancreatic and Duodenal Homeobox Gene 1 Induces Expression of Insulin Genes in Liver and Ameliorates Streptozotocin-Induced Hyperglycemia", Nature Medicine, 6(5): 568-572, 2000.			
	128	Benjamin et al. "A Plasticity Window for Blood Vessel Remodelling Is Defined by Pericyte Coverage of the Preformed Endothelial Network and Is Regulated by PDGF-B and VEGF", Development, 125: 1591-1598, 1998.			
	129	Vukicevic et al. "Induction of Nephrogenic Mesenchyme by Osteogenic Protein 1 (Bone Morphogenetic Protein 7)", Proc. Natl. Acad. Sci. USA, 93: 9021-9026, 1996.			
	130	Massague "The TGF-BETA Family of Growth and Differentiation Factors", Cell, 49: 437-438, 1987.			
	131	Pilbeam et al. "Comparison of the Effects of Various Lengths of Synthetic Human Parathyroid Hormone-Related Peptide (hPTHrP) of Malignancy on Bone Resorption and Formation in Organ Culture", Bone, 14: 717-720, 1993.			
	132	Skolnick et al. "From Genes to Protein Structure and Function: Novel Applications of Computational Approaches in the Genomic Era", Trends in Biotechnology, 18: 34-39, 2000.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

/Richard Hutson/ (09/25/2006)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO				Complete if Known	
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	7	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	133	Bork "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle", Genome Research, 10 : 398-400, 2000.			
	134	Doerks et al. "Protein Annotation: Detective Work for Function Prediction", Trends in Genetics, 14(6): 248-250, 1998.			
	135	Smith et al. "The Challenges of Genome Sequence Annotation or 'The Devil Is in the Details'", Nature Biotechnology, 15: 1222-1223, 1997.			
	136	Brenner "Errors in Genome Annotation", Trends in Genetics, 15(4): 132-133, 1999.			
	137	Bork "Go Hunting in Sequence Databases But Watch Out for the Traps", Trends in Genetics, 12(10): 425-427, 1996.			
	138	Bowie et al. "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions", Science, 247: 1306-1310, 1990.			
	139	Bendig et al. "Humanization of Rodent Monoclonal Antibodies by CDR Grafting", Methods in Enzymology, 8: 83-93, 1995.			
	140	Miao et al. "Cloning, Expression and Purification of Mouse Heparanase", Protein Expression and Purification, 26: 425-431, 2002.			
	141	Coligan et al. "Current Protocols in Immunology", Immunology - Laboratory Manuals, 1991.			
	142	Sasisekharan et al. "Cloning and Expression of Heparinase I Gene From Flavobacterium Heparinum", Proc. Natl. Acad. Sci. USA, 90: 3660-3664, 1993.			
	143	Gordon-Cardo et al. "Expression of Basic Fibroblast Growth Factor in Normal Human Tissues", Laboratory Investigation, 63: 832-840, 1990. Abstract.			
	144	Carson et al. Mucin and Proteoglycan Functions in Embryo Implantation", BioEssays, 20(7): 577-583, 1998. Abstract, P.580, Col.2, § 2, P.582, Col 1, Fig.1.			
	145	Novagen "PET System Manual", Novagen, 6th Ed., P.11, 1995.			
	146	Ennis et al. "Rapid Cloning of HLA-A,B cDNA by Using the Polymerase Chain Reaction: Frequency and Nature of Errors Produced in Amplification", PNAS USA, 87: 2833-2837, 1990.			
	147	Gilat et al. "Molecular Behaviour Adapts to Context: Heparanase Functions as An Extracellular Matrix-Degrading Enzyme or as A T-Cell Adhesion Molecule, Depending on the Local PH", Journal of Experimental Medicine, 181: 1929-1934, 1995.			
	148	Murphy et al. "The Latent Collagenase and Gelatin of Human Polymorphonuclear Neutrophil Leucocytes", Biochem. J., 192: 517-525, 1980.			
	149	Chubet et al. "Vectors for Expression and Secretion of FLAG Epitope-Tagged Proteins in Mammalian Cells", BioTechniques, 20: 136-141, 1996.			
	150	Chang et al. "Differential Ability of Heparan Sulfate Proteoglycans to Assemble the Fibroblast Growth Factor Receptor Complex In Situ", FASEB Journal, 14: 137-144, 2000.			
	151	Hillier et al. "The WashU-Merck EST Project", Database EMBL Accession No. N45367, XP 002198420, 1996. Abstract.			
	152	Marra et al. "The WashU-HHMI Mouse EST Project", Database EMBL, Accession No. A1122034, XP 002198426, 1998. Abstract.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>. Applicant's unique citation designation number (optional). <sup>2</sup>. Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount

/Richard Hutson/ (09/25/2006)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1448A/PTO				Complete if Known	
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	8	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	153	Marra et al. "The WashU-HHMI Mouse Est Project", Database EMBL, Accession No. AA047943, XP002198424, 1996.			
	154	Evans et al. "Human Chromosome 11 187a8 Cosmid, Complete Sequence", Database EMBL, Accession No. U73640, XP002198427, 1996. Abstract.			
	155	Suggs et al. "Use of Synthetic Oligonucleotides as Hybridization Probes: Isolation of Cloned cDNA Sequences for Human $\beta$ 2-Microglobulin", Proc. Natl. Acad. Ssci. USA, 78(11): 6613-6617, 1981. P.6613.			
	156	Ehle et al. "Immunoaffinity Chromatography of Enzymes", Bioseparation, 1(2): 97-110, 1990.			
	157	Nadav et al. "Activation, Processing and Trafficking of Extracellular Heparanase by Primary Human Fibroblasts", Journal of Cell Science, 115(10): 2179-2187, 2002.			
	158	Goldshmidt et al. "Cell Surface Expression and Secretion of Heparanase Markedly Promote Tumor Angiogenesis and Metastasis", Proc. Natl. Acad. Sci. USA, 99(15): 10031-10036, 2002.			
	159	Guo et al. "Protein Tolerance to Random Amino Acid Change", PNAS, 101(25): 9205-9210, 2004.			
	160	Dibrino "RT-PCR Method & Applications", Clontech Laboratories, 1st Ed., 1: 11, 15, 23, 41, 26, 1991.			
	161	Zcharia et al. "Heparanase Regulates Murine Hair Growth", American Journal of Pathology, 166(4): 999-1008, 2005.			
	162	Zhu et al. "Development of Heritable Melanoma in Transgenic Mice", The Journal of Investigative Dermatology, 110: 247-252, 1998.			
	163	Duff "Transgenic Mice Overexpressing Presenilin cDNAs: Phenotype and Utility in the Modeling of Alzheimer's Disease", Central Nervous System Diseases, P.123-128, 2000. Abstract.			
	164	Doetschman "Interpretation of Phenotype in Genetically Engineered Mice", Laboratory Animal Science, 49(2): 137-143, 1999.			
	165	Wall "Transgenic Livestock: Progress and Prospects for the Future", Theriogenology, 45: 57-68, 1996.			
	166	Mullins et al. "Fulminant Hypertension in Transgenic Rats Harboring the Mouse Ren-2 Gene", Nature, 344: 541-544, 1990.			
	167	Hammer et al. "Spontaneous Inflammatory Disease in Transgenic Rats Expressing HLA-B27 and Human $\beta$ 2m: An Animal Model of HLA-B27-Associated Human Disorders", Cell, 63: 1099-1112, 1990.			
	168	Taurog et al. "HLA-B27 in Inbred and Non-Inbred Transgenic Mice", The Journal of Immunology, 141(11): 4020-4023, 1988.			
	169	Pearce et al. "Development of Glucose Intolerance in Male Transgenic Mice Overexpressing Human Glycogen Synthase Kinase-3 $\beta$ on A Muscle-Specific Promoter", Metabolism, 53(10): 1322-1330, 2004.			
	170	Li et al. "In Vivo Fragmentation of Heparan Sulfate by Heparanase Overexpression Renders Mice Resistant to Amyloid Protein A Amyloidosis", PNAS, 102(18): 6473-6477, 2005.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount

/Richard Hutson/ (09/25/2006)



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1448A/PTO				Complete if Known	
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	9	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	171	Zcharia et al. "Heparanase Accelerates Wound Angiogenesis and Wound Healing in Mouse and Rat Models", The FASEB Journal, 19: 211-221, 2005.			
	172	Zcharia et al. "Molecular Properties and Involvement of Heparanase in Cancer Progression and Mammary Gland Morphogenesis", Journal of Mammary Gland Biology and Neoplasia, 6(3): 311-322, 2001.			
	173	Nadir et al. "Co- Interaction and Increased Release of Tissue Factor Pathway Inhibitor by Heparanase", Blood, 106(11/Part 2): 90B, 2005. Abstract# 4038.			
	174	Spiegel et al. "Heparanase Facilitates Development and SDF-1 Induced Migration of Hematopoietic Stem and Progenitor Cells", Blood, 102(11): 825a-826a, 2003. Abstract# 3056.			
	175	Zcharia et al. "Transgenic Expression of Mammalian Heparanase Uncovers Physiological Functions of Heparan Sulfate in Tissue Morphogenesis, Vascularization, and Feeding Behavior", The FASEB Journal, 18: 252-263, 2004.			
	176	Nasser et al. "Heparanase Neutralizes the Anticoagulation Properties of Heparin and Low-Molecular-Weight Heparin", Journal of Thrombosis and Haemostasis, 4: 560-565, 2006.			
	177	Mullins et al. "Expression of the DBA/2J Ren-2 Gene in the Adrenal Gland of Transgenic Mice", The EMBO Journal, 8(13): 4065-4072, 1989.			
	178	McKenzie et al. "Biochemical Characterization of the Active Heterodimer Form of Human Heparanase (Hpa1) Protein Expressed in Insect Cells", Biochemical Journal, 373: 423-435, 2003.			
	179	McKenzie et al. "Biochemical Characterization of the Active Heterodimer Form of Human Heparanase (Hpa1) Protein Expressed in Insect Cells", Biochemical Journal, 373:423-436, 2003.			
	180	Vlodavsky et al. "Lymphoma Cell-Mediated Degradation of Sulfated Proteoglycans in the Subendothelial ExtraCellular Matrix: Relationship to Tumor Cell Metastasis", Cancer Research, 43: 2704-2711, 1983.			
	181	Vlodavsky et al. "Morphological Appearance, Growth Behaviour and Migratory Activity of Human Tumor Cells Maintained on Extracellular Matrix Versus Plastic", Cell, 19: 607-616, 1980.			
	182	Miao et al. "Modulation of Fibroblast Growth Factor-2 Receptor Binding Dimerization, Signaling, and Angiogenic Activity by A Synthetic Heparin-Mimicking Polyaromatic Compound", J. Clin. Invest., 99(7): 1565-1575, 1997.			
	183	Benezra et al. "Reversal of Fibroblast Growth Factor-Mediated Autocrine Cell Transformation by Aromatic Anionic Compounds", Cancer Research, 52: 5656-5662, 1992.			
	184	Irimura et al. "Chemically Modified Heparins as Inhibitors of Heparan Sulfate Specific Endo-β-Glucuronidase (Heparanase) of Metastatic Melanoma Cells", Biochemistry, 25: 5322-5328, 1986. Abstract.			
	185	Coombe et al. "Analysis of the Inhibition of Tumor Metastasis by Sulphated Polysaccharides", Int. J. Cancer, 39: 82-88, 1987. Abstract.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>. Applicant's unique citation designation number (optional). <sup>2</sup>. Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO  <b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Complete if Known		
				Application Number	09/978,297	
				Filing Date	October 17, 2001	
				First Named Inventor	Oron JACOBY-ZEEVI	
				Group Art Unit	1652	
Examiner Name	HUTSON, RICHARD G					
Sheet	10	OF	15	Attorney Docket Number 01/22716		
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS						
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.				T <sup>2</sup>
RH	186	Ornitz et al. "Heparin Is Required for Cell-Free Binding of Basic Fibroblast Growth Factor to A Soluble Receptor and for Mitogenesis in Whole Cells", Molecular and Cellular Biology, 12: 240-247, 1992.				
	187	Aviezer et al. "Differential Structural Requirements of Heparin and Heparan Sulfate Proteoglycans That Promote Binding of Basic Fibroblast Growth Factor to Its Receptor", J. Biol. Chem., 269(1): 114-121, 1994.				
	188	Bartlett et al. "Comparative Analysis of the Ability of Leucocytes, Endothelial Cells, and Platelets to Degrade the Subendothelial Basement Membrane: Evidence for Cytokine Dependence and Detection of A Novel Sulfatase", Immunology and Cell Biol., 73: 113-124, 1995.				
	189	Nakajima et al. "A Solid-Phase Substrate of Heparanase: Its Application to Assay of Human Melanoma for Heparan Sulfate Degradative Activity", Analytical Biochemistry, 157: 162-171, 1986.				
	190	Oosta et al. "Purification and Properties of Human Platelets Heparitanase", J. Biol. Chem., 257(19): 11249-11255, 1982.				
	191	Sewell et al. "Human Mononuclear Cells Contain An Endoglycosidase Specific for Heparan Sulfate Glycosaminoglycan Demonstrable With the Use of A Specific Solid-Phase Metabolically Radiolabelled Substrate", Biochem J., 264: 777-783, 1989.				
	192	Freeman et al. "A Rapid Quantitative Assay for the Detection of Mammalian Heparanase Activity", Biochemical Journal, 325: 229-237, 1997.				
	193	Taylor et al. "A Colorimetric Method for the Quantitation of Uronic Acids and A Specific Assay for Galacturonic Acid", Analytical Biochemistry, 201: 190-196, 1992.				
	194	Basu et al. "Analysis of Glycosphingolipids by Fluorophore-Assisted Carbohydrate Electrophoresis Using Ceramide Glycanase From Mercenaria Mercenaria", Analytical Biochemistry, 222: 270-274, 1994.				
	195	Jackson "The Use of Polyacrylamide-Gel Electrophoresis for the High-Resolution of Separation of Reducing Saccharides Labelled With the Fluorophore 8-Aminonaphtalene-1, 3, 6-Trisulphonic Acid", Biochem J., 270: 705-713, 1990.				
	196	De Vouge et al. "Immunoselection of GRP94/Endoplasmic Reticulum From A KNRK Cell-Specific $\lambda$ gt11 Library Using Antibodies Directed Against A Putative Heparanase Amino-Terminal Peptide", Int. J. Cancer, 56: 286-294, 1994. IDS in 26871; IDS in 25718; Suppl. IDS in 23884;				
	197	Mollinedo et al. "Major Co-Localization of the Extracellular-Matrix Degradative Enzymes Heparanase and Gelatinase in Tertiary Granules of Human Neutrophils", Biochemical Journal, 327: 917-923, 1997. IL/OA of 15.1.06 in 20462; Suppl. IDS in 23884;				
	198	Hudson "Recombinant Antibody Fragment", Curr. Opin. Biotech., 4:395-402, 1998. Abstract.				

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria

/Richard Hutson/ (09/25/2006)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1448A/PTO				Complete if Known	
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	11	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	199	Schoepe et al. "Neutralization of Hemolytic and Mouse Lethal Activities of C. Perfringens Alpha-Toxin Need Simultaneous Blockage of Two Epitopes by Monoclonal Antibodies", Microb. Pathogenesis, 23(1): 1-10, 1997. Abstract.			
	200	Ngo et al. "Computational Complexity, Protein Structure Prediction, and the Levinthal Paradox", The Protein Folding Problem and Tertiary Structure Prediction, Birkhauser, Boston, P.433, 492-495, 1994. Suppl. IDS in 23884;			
	201	Colman "Effects of Amino Acid Sequence Changes on Antibody-Antigen Interactions", Research in Immunology, 145(1): 33-36. 1994.			
	202	Abaza et al. "Effects of Amino Acid Substitutions Outside An Antigenic Site on Protein Binding to Monoclonal Antibodies of Predetermined Specificity Obtained by Peptide Immunization: Demonstration With Region 94-100 (Antigenic Site 3) of Myoglobin", Journal of Protein Chemistry, 11(5): 433-444, 1992.			
	203	Lederman et al. "A Single Amino Acid Substitution in A Common African Allele of the CD4 Molecule Ablates Binding of the Monoclonal Antibody, OKT4", Molecular Immunology, 28: 1171-1181, 1991.			
	204	Li et al. "β-Endorphin Omission Analogs: Dissociation of Immunoreactivity From Other Biological Activities", PNAS, 77: 3211-3214, 1980.			
	205	Marchetti et al. "Neurotrophin Stimulation of Human Melanoma Cell Invasion: Selected Enhancement of Heparanase Activity and Heparanase Degradation of Specific Heparan Sulfate Subpopulations", Cancer Research, 56: 2856-2863, 1996. Also in: Advances in Enzyme Regulation, 37: 111-134, 1997. // Suppl. IDS in 23884;			
	206	Kosir et al. "Human Prostate Carcinoma Cells Produce Extracellular Heparanase", Journal of Surgical Research, 67: 98-105, 1997. EP/OA of 1.10.01 in 20458; S18 in 21782; S18 in 20462; Notice of Allowability of 28.12.05 in 21205; IL/OA of 15.1.06 in 20462; IDS in 26871; IDS in 25718; Suppl. IDS in 23884;			
	207	Köhler et al. "Continuous Cultures of Fused Cells Secreting Antibody of Predetermined Specificity", Nature, 256: 495-497, 1975.			
	208	Hulett et al. "Cloning of Mammalian Heparanase, An Important Enzyme in Tumor Invasion and Metastasis", Nature Medicine, 5(7): 803-809, 1999.			
	209	Toyoshima et al. "Human Heparanase: Purification, Characterization, Cloning, and Expression", J. Biolog. Chemistry, 274(34): 24153-24160, 1999.			
	210	Kussie et al. "Cloning and Functional Expression of A Human Heparanase Gene", Biochemical and Biophysical Research Communication, 261(1): 183-187, 1999.			
	211	Walch et al. "Correlation of Overexpression of the Low-Affinity p75 Neurotrophin Receptor With Augmented Invasion and Heparanase Production in Human Malignant Melanoma Cells", Int. J. Cancer, 82: 112-120, 1999.			
	212	Freeman et al. "Evidence That Platelet and Tumour Heparanases Are Similar Enzymes", Biochem J., 342: 361-368, 1999.			
	213	Zhou et al. "A 182 Bp Fragment of the Mouse Proα1(11) Collagen Gene Is Sufficient to Direct Chondrocyte Expression in Transgenic Mice", J. Cell Science, 108: 3677-3684, 1995.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>. Applicant's unique citation designation number (optional). <sup>2</sup>. Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria

/Richard Hutson/ (09/25/2006)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO				Complete if Known	
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	12	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	214	Hormuzdi et al. "A Gene-Targeting Approach Identifies A Function for the First Intron in Expression of the $\alpha 1$ (I) Collagen Gene.", Mol Cell Biol., 18(6): 3368-3375, 1998. Abstract.			
	215	Chow et al. "Development of An Epithelium-Specific Expression Cassette With Human DNA Regulatory Elements for Transgene Expression in Lung Airways", Proc. Natl. Acad. Sci. USA, 94: 14695-14700, 1997.			
	216	Ye et al. "Targeted Gene Correction: A New Strategy for Molecular Medicine", Molecular Medicine Today, P.431-437, 1998.			
	217	Lai et al. "Homologous Recombination Based Gene Therapy", Exp. Nephrol, 7(1):11-14, 1999. Abstract.			
	218	Yazaki et al. "The Structure and Expression of the FGF Receptor-1 mRNA Isoforms in Rat Tissues", Biochimica et Biophysica Acta, 1172: 37-42, 1993.			
	219	Le Fur et al. "Selective Increase in Specific Alternative Splice Variants of Tyrosinase in Murine Melanomas: A Projected Basis for Immunotherapy", Proc. Natl. Acad. Sci. USA, 94: 5332-5337, 1997.			
	220	Gewirtz et al. "Nucleic Acid Therapeutics: State of the Art and Future Prospects", Blood, 92(3): 712-736, 1998.			
	221	Shastri "Gene Disruption in Mice: Models of Development and Disease", Molecular and Cellular Biochemistry, 181: 163-179, 1998.			
	222	Carpentier et al. "DNA Vaccination With HuD Inhibits Growth of A Neuroblastoma in Mice", Clinical Cancer Research, 4: 2819-2824, 1998.			
	223	Lai et al. "DNA Vaccines", Critical Reviews in Immunology, 18: 449-484, 1998.			
	224	Kurachi et al. "Role of Intron I in Expression of the Human Factor IX Gene", Journal of Biological Chemistry, 270(10): 5276-5281, 1995.			
	225	Shekhar et al. "Correlation of Differences in Modulation of Ras Expression With Metastatic Competence of Mouse Mammary Tumour Subpopulations", Invasion Metastasis, 14: 27-37, 1994/5.			
	226	Durand et al. "Active-Site Motifs of Lysosomal Acid Hydrolases: Invariant Features of Clan GH-A Glycosyl Hydrolases Deduced From Hydrophobic Cluster Analysis", Glycobiology, 7(2): 277-284, 1997.			
	227	Korb et al. "Stimulation of Gene Expression by Introns: Conversion of An Inhibitory Intron to A Stimulatory Intron by Alteration of the Splice Donor Sequence", Nucleic Acids Research, 21(25): 5901-5908, 1993.			
	228	Fairbanks et al. "Processing of the Human Heparanase Precursor and Evidence that the Active Enzyme Is A Heterodimer", The Journal of Biological Chemistry, 274(42): 29587-29590, 1999.			
	229	Linhardt et al. "Polysaccharide Lyases", Applied Biochemistry and Biotechnology, 12: 135-176, 1986.			
	230	Dempsey et al. "Heparanase, A Potential Regulator of CellMatrix Interactions", TIBS, 25(8): 349-351, 2000. P.350, Col.1, § 1, Col.3, § 1, Claims 1-24.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>. Applicant's unique citation designation number (optional). <sup>2</sup>. Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of commerce, P.O. Box 1450, Alexandria

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO				Complete if Known	
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	13	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	231	Niwa et al. "Efficient Selection for High-Expression Transfectants With A Novel Eukaryotic Vector", Gene, 108(2): 193-199, 1991. Abstract.			
	232	Mirault et al. "Transgenic Glutathione Peroxidase Mouse Models for Neuroprotection Studies", Ann. NY Acad. Sci., 738: 104-115, 1994. Abstract.			
	233	Lampard et al. "Secretion of Foreign Proteins Mediated by Chicken Lysozyme Gene Regulatory Sequences", Biochem. Cell Biol., 80(6): 777-788, 2002. Abstract.			
	234	Morrison et al. "Sequences in Antibody Molecules Important for Receptor-Mediated Transport Into the Chicken Egg Yolk", Mol. Immunol., 38(8): 619-625, 2002.			
	235	Richards et al. "Construction and Preliminary Characterization of the Rat Casein and Alpha-Lactalbumin cDNA Clones", J. Biol. Chem., 256(1): 526-32, 1981.			
	236	Campbell et al. "Comparison of the Whey Acidic Protein Genes of the Rat and Mouse", Nucleic Acids Res., 12(22): 8685-8697, 1984.			
	237	Gorodetsky et al. "Isolation and Characterization of the Bos Taurus $\beta$ -Casein Gene", Gene, 66: 87-96, 1988. Abstract.			
	238	Benezra et al. "Thrombin Enhances the Degradation of Heparan Sulfate in the Extracellular Matrix by Tumor Cell Heparanase", Exptl. Cell. Res., 201: 208-215, 1992.			
	239	Harlow et al. "Antibodies - A Laboratory Manual", Cold Spring Harbor Press, P. 471-510, 1988.			
	240	Wang "Basic Fibroblast Growth Factor Infused at Different Times During Bone Graft Incorporation. Titanium Chamber Study in Rats", Acta Orthop. Scand., 67(3): 229-236, 1996. Abstract.			
	241	Matoba et al. "Evaluation of Omental Implantation for Perforated Gastric Ulcer Therapy: Findings in A Rat Model", J. Gastroenterol., 31(6): 777-784, 1996. Abstract.			
	242	Smith et al. "Expression of Heparan Sulfate Protoglycan (Perlecan) in the Mouse Blastocyst Is Regulated During Normal and Delayed Implantation", Dev. Biol., 184(1): 38-47, 1997. Abstract.			
	243	Richardson et al. "Regulation of Basic Fibroblast Growth Factor Binding and Activity by Cell Density and Heparan Sulfate", J. Biological Chemistry, 274(19): 13534-13540, 1990.			
	244	Hayward et al. "Cellular Mechanisms of Heparinase III Protection in Rat Traumatic Shock", American Journal of Physiology, 275: H23-H30, 1998.			
	245	Sasisekharan et al. "Heparinase Inhibits Neovascularization", Proc. Natl. Acad. Sci. USA, 91: 1524-1528, 1994.			
	246	Whitelock et al. "The Degradation of Human Endothelial Cell-Derived Perlecan and Release of Bound Basic Fibroblast Growth Factor by Stromelysin, Collagenase, Plasmin, and Heparanases", Journal of Biological Chemistry, 271(17): 10079-10086, 1996.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria

/Richard Hutson/ (09/25/2006)

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1448A/PTO				Complete if Known	
<b>SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(use as many sheets as necessary)</i>				Application Number	09/978,297
				Filing Date	October 17, 2001
				First Named Inventor	Oron JACOBY-ZEEVI
				Group Art Unit	1652
				Examiner Name	HUTSON, RICHARD G
Sheet	14	OF	15	Attorney Docket Number	01/22716
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.			T <sup>2</sup>
RH	247	Godder et al. "Heparanase Activity in Cultured Endothelial Cells", Journal of Cellular Physiology, 148: 274-280, 1991.			
	248	Kato et al. "Physiological Degradation Converts the Soluble Syndecan-1 Ectodomain From An Inhibitor to A Potent Activator of FGF-2", Nature Medicine, 4(6): 691-697, 1998.			
	249	Jin et al. "Immunohistochemical Localization of Heparanase in Mouse and Human Melanomas", International Journal of Cancer, 45: 1088-1095, 1990. EP/OA of 27.10.05 in 22371; S18 in 20470; S18 in 20462; IL/OA of 15.1.06 in 20462; Suppl. IDS in 27970; IDS in 26871; IDS in 25718; Suppl. IDS in 23884;			
	250	Hoogewerf et al. "CXC Chemokines Connective Tissue Activating Peptide-III and Neutrophil Activating Peptide-2 Are Heparin/Heparan Sulfate-Degrading Enzymes", Journal of Biological Chemistry, 270(7): 3268-3277, 1995.P.3269 Suppl. IDS in 27970; IDS in 26871; IDS in 25718; Suppl. IDS in 23884;			
	251	Oldberg et al. "Characterization of A Platelet Endoglycosidase Degrading Heparin-Like Polysaccharides", Biochemistry, 19: 5755-5762, 1980.			
	252	Miyake et al. "Highly Specific and Sensitive Detection of Malignancy in Urine Samples From Patients With Urothelial Cancer by CD44v8-10/CD44v10 Competitive RT-PCR", Int. J. Cancer, 79(6): 560-564, 1998. Abstract.			
	253	Kang et al. "Prolactin-Inducible Enhancer Activity of the First Intron of the Bovine $\beta$ -Casein Gene", Mol. Cells, 8(3): 259-265, 1998. Abstract.			
	254	Gottschalk et al. "Somatic Gene Therapy. Present Situation and Future Perspective", Arzneimittelforschung, 48(11): 1111-1120, 1998. Abstract.			
	255	Guriec et al. "CD44 Isoforms With Exon V6 and Metastasis of Primary N0M0 Breast Carcinomas", Breast Cancer Res. Treat., 44(3):261-268, 1997. Abstract.			
	256	Hida et al. "Antisense E1AF Transfection Restrains Oral Cancer Invasion by Reducing Matrix Metalloproteinase Activities", Am. J. Pathol., 50(6): 2125-2132, 1997. Abstract.			
	257	Vlodavsky et al. "Mammalian Heparanase: Gene Cloning, Expression and Function in Tumor Progression and Metastasis", Nature Medicine, 5(7): 793-802, 1999. IDS in 26871; IDS in 25718;			
	258	Faber-Elman et al. "Involvement of Wound-Associated Factors in Rat Brain Astrocyte Migratory Response to Axonal Injury: In Vitro Simulation", J. Clin. Invest., 97(1): 162-171, 1996.			
	259	Zheng et al. "Increment of hFIX Expression With Endogenous Intron I In Vitro", Cell Res., 7(1):21-29, 1997 Abstract.			
	260	Welch et al. "Expression of Ribozymes in Gene Transfer Systems to Modulate Target RNA Levels", Curr. Opin. Biotechnol., 9(5): 486-496, 1998. Abstract.			
	261	Gewirtz et al. "Facilitating Oligonucleotide Delivery: Helping Antisense Deliver on Its Promise", Proc. Natl. Acad. Sci. USA, 93: 3161-3163, 1996.			
	262	Green et al. "Antisense Oligonucleotides: An Evolving Technology for the Modulation of Gene Expression in Human Disease", Journal of American Cell Surgery, 191(1): 93-105, 2000.			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>. Applicant's unique citation designation number (optional). <sup>2</sup>. Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including

